REMARKS

The claims have been amended to claim the invention more explicitly, and the amendments are believed to conform to the discussion at the interview. Independent claims 1 and 10 have been amended and recite that the specified gene is that which encodes the protein of SEQ. ID. NO: 2 (Figure 1). This is important, because, according to Wong, the protein of this sequence is a suppressor protein which would not be expected to be found in tumors, contrary to applicants' results. The mutated forms of this sequence are, however, possibly found in these tumors - *i.e.*, mutants which have lost their suppressor function. New claims 48-61 parallel the language of the currently pending claims, however, they are directed to the cDNA clone 20P1F12-GTC1 contained in the plasmid deposited with the ATCC as Accession No. 207097 referenced in the specification, for example at page 5, line 30, this cDNA clone encodes the 20P1F12/TMPRSS2 protein. The remaining amendments to the claims are of a clerical nature and do not introduce new matter. Thus, no new matter has been added and entry of the amendment is respectfully requested.

Upon entry of the new claims, claims 1-3, 5-7, 10-13, 15, 17-19 and 48-61 will be pending.

Formal Matters

The specification has been amended to indicate the status of the applications from which priority is claimed and the asserted hyperlinks have been removed.

With respect to the ATCC information requested by the Office, the hybridomas referenced on pages 39 and 40 of the specification are being deposited with the ATCC. This deposit is in accordance with the provisions of The Budapest Treaty and with 37 C.F.R. §§ 1.801

through 1.809. Applicants submit that these deposits will be available upon the indication of allowable subject matter in the present application. Accordingly, as this objection relates to form not necessary for further consideration of the present claims, applicants respectfully request that the Office hold this requirement in abeyance until allowable subject matter in this application is indicated. See 37 C.F.R. § 1.111(b).

The Office has also objected to the specification for improper disclosure of amino acid sequences without a respective sequence identifier. In this regard, applicants will shortly submit a supplemental response including the required sequence listing in accordance with the requirements of 37 C.F.R. §§ 1.821 through 1.825. As this objection relates to form not necessary for further consideration of the present claims, applicants respectfully request that the Office hold this requirement in abeyance until an updated, computer-readable form (CRF) of the sequence listing is provided. See 37 C.F.R. § 1.111(b).

Priority Date

Applicants note the Office considers the present claims entitled only to a priority from April 14, 1999. Applicants do not contest this determination at this time, as assignment of this priority has no bearing on the present rejections and is not relevant to any art of which applicants are currently aware. Applicants reserve their right to raise this issue should it become relevant.

The Rejections Under 35 U.S.C. § 112, paragraph 2

Claims 1, 3-9 and 17-19 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite. First, the Office objects, in claims 1 and 4-7, to the recitation of "status of 20P1F12/TMPRSS2." It is believed that this has been clarified by the amendment to the claims. It is intended that the expression levels of this gene are measured.

Claim 3 is rejected as vague concerning terminology regarding "immunoreactive complex." It is believed this is clarified by amendment as well. With the rewriting of the claim, the meaning of "immunocomplex" should be clear, but has been made explicit.

Claims 8-9 and 17-19 were rejected as vague for reciting a "binding partner." Amendment has clarified this to read "an antibody or fragment thereof immunoreactive with said protein."

It is believed that the amendments to the claims are responsive to all rejections under this section of the statute.

Status of Claims

In view of the amendments, it is believed that claims 6, 11, and 19 are in a position for immediate allowance. None of these claims was rejected over the art. Claim 11 was merely objected to but considered allowable if rewritten in independent form. Accordingly, it is clear that at least claims 6, 11 and 19 are allowable.

The Rejection Over the Art

The remaining claims, claims 1-3, 5, 7, 10, 12-13, 15, and 17-18 were rejected as putatively anticipated by Wong under 35 U.S.C. § 102(e).

Applicants respectfully submit that the teachings of Wong were misinterpreted. There is absolutely no evidence in Wong that the production of the designated protein in a tissue is characteristic of tumor cell growth or neoplasia, or that the protein is produced at all. In fact, Wong appears to teach exactly the opposite. At column 10, lines 53-57, Wong states

> Mutations which interfere with the function of the TMPRSS2 gene product are involved in the pathogenesis of cancer. Thus, the presence of an altered (or mutant) TMPRSS2 gene which produces

> a protein having a loss of function, or altered function, or the lack of this protein, directly increases the risk of cancer.

Thus, Wong teaches that it is the lack of expression of the relevant gene that would be associated with cancer.

While Wong describes in prophetic terms production of the protein and analysis of samples using this protein, there is no evidence in Wong that the protein is actually produced. Indeed, the granted claim in Wong is limited to DNA comprising polymorphic variants. But more significantly, the analysis of Wong is directed to finding variants of the protein not the designated protein itself. It is the presence of these variants which Wong contends are indicative of tumor formation; according to Wong, the native protein would occur in normal tissues.

Thus, far from rendering the present invention obvious, Wong actually teaches away from the invention as presently claimed.

For the reasons set forth above, the rejection under 35 U.S.C. § 102(e) may properly be withdrawn.

CONCLUSION

The claims have been amended for clarification. The amended claims are free of the rejection under 35 U.S.C. § 112, paragraph 2; this was the only basis for rejection of claims 6 and 19. As claims 6, 11 and 19 were not rejected over the art, and clarifying amendments have been made, these claims should immediately be considered allowable. The remaining claims are patentable over the art as well in view of the complete lack of evidence in Wong that any protein is produced and in view of the teaching of Wong that lack of the gene encoding this protein predisposes the subject to development of neoplasms.

In the event there are outstanding issues which the Examiner believes can be resolved through a telephone conversation, a telephone call to the undersigned is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 511582000820.

Respectfully submitted,

Dated: June 10, 2002

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EXHIBIT A. - MARKED-UP VERSION OF AMENDMENTS TO THE SPECIFICATION AND CLAIMS

In the Specification:

Please add the below subheading and amend the paragraph, under the title, on page 1, lines 4-8, as following:

Cross-Reference to Related Applications

This application is a continuation-in-part application of U.S. Ser. No. 09/323,597 filed June 1, 1999 which claims the benefit of United States provisional patent application serial numbers 60/087,598, filed June 1, 1998, now lapsed, 60/091,474 filed June 29, 1998, now lapsed and 60/129,521, filed April 14, 1999, now lapsed. The entire contents of these provisional and non-provisional patent applications are incorporated by reference into this application.

Please amend the paragraph from page 16, line 32 through page 17, line 7 as follows:

In the context of amino acid sequence comparisons, the term "identity" is used to express the percentage of amino acid residues at the same relative positions that are the same. Also in this context, the term "homology" is used to express the percentage of amino acid residues at the same relative positions that are either identical or are similar, using the conserved amino acid criteria of BLAST analysis, as is generally understood in the art. For example, % identity values may be generated by WU-BLAST-2 (Altschul et al., 1996, Methods in Enzymology 266:460-480; available at http[://] address "blast.wustl/edu/blast/README.html"). Further details regarding amino acid substitutions, which are considered conservative under such criteria, are provided below.

Please amend the paragraph from page 31, lines 21-31 as follows:

Redundancy in the genetic code permits variation in 20P1F12/TMPRSS2 gene sequences. In particular, one skilled in the art will recognize specific codon preferences by a specific host species and can adapt the disclosed sequence as preferred for a desired host. For example, preferred codon sequences typically have rare codons (i.e., codons having a usage frequency of less than about 20% in known sequences of the desired host) replaced with higher frequency codons. Codon preferences for a specific organism may be calculated, for example, by utilizing codon usage tables available on the Internet at the following address: [http://] "www.dna.affrc.go.jp/~nakamura/codon.html." Nucleotide sequences that have been optimized for a particular host species by replacing any codons having a usage frequency of less than about 20% are referred to herein as "codon optimized sequences."

In the Claims:

1. (Twice amended) A method of examining a biological sample for evidence of [dysregulated cellular] tumor cell growth comprising comparing the [status] expression level of the 20P1F12/TMPRSS2 gene, which encodes the protein of SEQ. ID. NO: 2 (Figure 1), in the biological sample to the [status] expression of said 20P1F12/TMPRSS2 gene in a corresponding normal sample, wherein [alterations in the status] enhancement of the level of 20P1F12/TMPRSS2 expression in the biological sample [are associated with] is evidence of [dysregulated cellular] tumor cell growth.

2. (Amended) The method according to claim 1, wherein the [status] level of expression of the 20P1F12/TMPRSS2 gene in the biological sample is evaluated by examining [levels of 20P1F12/TMPRSS2 mRNA expression or levels] the level of 20P1F12/TMPRSS2 protein[expression] produced.

3. (Amended) The method according to claim [1] 2, wherein the [status] level of 20P1F12/TMPRSS2 protein in the biological sample is evaluated by contacting the sample with antibody or fragment thereof immunoreactive with said protein, and observing the presence or

absence of an [20P1F12/TMPRSS2] immuno[reactive]complex formed from the antibody or fragment with any 20P1F12/TMPRSS2 protein.

6. (Twice amended) The method according to claim 1, wherein the [dysregulated cellular] tumor cell growth is indicative of a prostate cancer.

7. (Twice amended) The method according to claim 1, wherein the [dysregulated cellular] tumor cell growth is indicative of a colon cancer.

10. (Amended) A method of identifying evidence of a neoplasm in a biological sample comprising:

(a) examining a level of expression of 20P1F12/TMPRSS2 gene [expression] , which encodes the protein of SEQ. ID. NO: 2 (Figure 1), in a test biological sample; and

(b) comparing the level of said 20P1F12/TMPRSS2 gene expression in the test biological sample to a level of said 20P1F12/TMPRSS2 gene expression found in a comparable normal biological sample,

wherein [differences in the] an enhanced level of said 20P1F12/TMPRSS2 gene products in the test biological sample relative to the normal biological sample [are associated with the] is evidence of a neoplasm.

15. (Amended) The method according to claim 10, wherein the level of 20P1F12/TMPRSS2 gene expression in the test biological sample is evaluated by examining the level of 20P1F12/TMPRSS2 protein[expression].

17. (Amended) The method of claim [10] 15, wherein the level of 20P1F12/TMPRSS2 [gene expression in a test biological sample] protein is evaluated by an immunoassay by contacting the sample with antibody or fragment thereof immunoreactive with said protein and observing the presence or absence of an immunocomplex [which measures the concentration of free 20P1F12/TMPRSS2 polypeptide or the concentration of 20P1F12/TMPRSS2 polypeptide complexed to a binding partner] formed from the antibody or fragment with any 20P1F12/TMPRSS2 protein.

18. (Amended) The method of claim [17] 10, wherein the 20P1F12/TMPRSS2 evaluated in the test biological sample is secreted from neoplastic cells [exhibiting disregulated growth].

19. (Amended) The method of claim 18, wherein the neoplastic cells [exhibiting disregulated growth] are prostate cancer cells.

EXHIBIT B. CURRENTLY PENDING CLAIMS AFTER ENTRY OF THE PRESENT AMENDMENT

1. (Twice amended) A method of examining a biological sample for evidence of tumor cell growth comprising comparing the expression level of the 20P1F12/TMPRSS2 gene, which encodes the protein of SEQ. ID. NO: 2 (Figure 1), in the biological sample to the expression of said 20P1F12/TMPRSS2 gene in a corresponding normal sample, wherein enhancement of the level of 20P1F12/TMPRSS2 expression in the biological sample is evidence of tumor cell growth.

2. (Amended) The method according to claim 1, wherein the level of expression of the 20P1F12/TMPRSS2 gene in the biological sample is evaluated by examining the level of 20P1F12/TMPRSS2 protein produced.

3. (Amended) The method according to claim 2, wherein the level of 20P1F12/TMPRSS2 protein in the biological sample is evaluated by contacting the sample with antibody or fragment thereof immunoreactive with said protein, and observing the presence or absence of an immunocomplex formed from the antibody or fragment with any 20P1F12/TMPRSS2 expressed protein.

5. The method according to claim 1, wherein the biological sample is selected from the group consisting of blood, serum, stool, urine, semen and biopsied tissue.

6. (Twice amended) The method according to claim 1, wherein the tumor cell growth is indicative of a prostate cancer.

7. (Twice amended) The method according to claim 1, wherein the tumor cell growth is indicative of a colon cancer.

10. (Amended) A method of identifying evidence of a neoplasm in a biological sample comprising:

(a) examining a level of expression of 20P1F12/TMPRSS2 gene, which encodes the protein of SEQ. ID. NO: 2 (Figure 1), in a test biological sample; and

(b) comparing the level of said 20P1F12/TMPRSS2 gene expression in the test biological sample to a level of said 20P1F12/TMPRSS2 gene expression found in a comparable normal biological sample,

wherein an enhanced level of said 20P1F12/TMPRSS2 gene products in the test biological sample relative to the normal biological sample is evidence of a neoplasm.

11. The method according to claim 10, wherein the neoplasm is a prostate cancer.

12. The method according to claim 10, wherein the neoplasm is a colon cancer.

13. The method according to claim 10, wherein the test biological sample is selected from the group consisting of blood, serum, stool, urine, semen and biopsied tissue.

15. (Amended) The method according to claim 10, wherein the level of 20P1F12/TMPRSS2 gene expression in the test biological sample is evaluated by examining the level of 20P1F12/TMPRSS2 protein.

17. (Amended) The method of claim 15, wherein the level of 20P1F12/TMPRSS2 protein is evaluated by an immunoassay by contacting the sample with antibody or fragment thereof immunoreactive with said protein and observing the presence or absence of an immunocomplex formed from the antibody or fragment with any 20P1F12/TMPRSS2 protein.

18. (Amended) The method of claim 10, wherein the 20P1F12/TMPRSS2 evaluated in the test biological sample is secreted from neoplastic cells.

19. (Amended) The method of claim 18, wherein the neoplastic cells are prostate cancer cells.

48. (New) A method of examining a biological sample for evidence of tumor cell growth comprising comparing the expression level of the 20P1F12/TMPRSS2 gene, which encodes the protein encoded by a cDNA clone 20P1F12-GTC1 contained in the plasmid deposited with the American Type Culture Collection (ATCC) as Accession No. 207097, in the biological sample to the expression of said 20P1F12/TMPRSS2 gene in a corresponding normal sample, wherein enhancement of the level of 20P1F12/TMPRSS2 expression in the biological sample is evidence of tumor cell growth.

49. (New) The method according to claim 48, wherein the level of expression of the 20P1F12/TMPRSS2 gene in the biological sample is evaluated by examining the level of 20P1F12/TMPRSS2 protein produced.

50. (New) The method according to claim 49, wherein the level of 20P1F12/TMPRSS2 protein in the biological sample is evaluated by contacting the sample with antibody or fragment thereof immunoreactive with said protein, and observing the presence or absence of an immunocomplex formed from the antibody or fragment with any 20P1F12/TMPRSS2 protein.

51. (New) The method according to claim 48, wherein the biological sample is selected from the group consisting of blood, serum, stool, urine, semen and biopsied tissue.

52. (New) The method according to claim 48, wherein the tumor cell growth is indicative of a prostate cancer.

53. (New) The method according to claim 48, wherein the tumor cell growth is indicative of a colon cancer.

54. (New) A method of identifying evidence of a neoplasm in a biological sample comprising:

(a) examining a level of expression of 20P1F12/TMPRSS2 gene, which encodes the protein encoded by a cDNA clone 20P1F12-GTC1 contained in the plasmid deposited with the

American Type Culture Collection (ATCC) as Accession No. 207097, in a test biological sample; and

(b) comparing the level of said 20P1F12/TMPRSS2 gene expression in the test biological sample to a level of said 20P1F12/TMPRSS2 gene expression found in a comparable normal biological sample,

wherein an enhanced level of said 20P1F12/TMPRSS2 gene products in the test biological sample relative to the normal biological sample is evidence of a neoplasm.

55. (New) The method according to claim 54, wherein the neoplasm is a prostate cancer.

56. (New) The method according to claim 54, wherein the neoplasm is a colon cancer.

57. (New) The method according to claim 54, wherein the test biological sample is selected from the group consisting of blood, serum, stool, urine, semen and biopsied tissue.

58. (New) The method according to claim 54, wherein the level of 20P1F12/TMPRSS2 gene expression in the test biological sample is evaluated by examining the level of 20P1F12/TMPRSS2 protein.

59. (New) The method of claim 58, wherein the level of 20P1F12/TMPRSS2 protein is evaluated by an immunoassay by contacting the sample with antibody or fragment thereof immunoreactive with said protein and observing the presence or absence of an immunocomplex formed from the antibody or fragment with any 20P1F12/TMPRSS2 protein.

60. (New) The method of claim 54, wherein the 20P1F12/TMPRSS2 evaluated in the test biological sample is secreted from neoplastic cells.

61. (New) The method of claim 60, wherein the neoplastic cells are prostate cancer cells.